I. Allowable Subject Matter

Applicants note with appreciation that the Examiner found Claim 4 to be allowable.

II. The Rejections

A. The Rejection of Claims 1 And 2 Over Evans And The '834 Patent Under 35 U.S.C. §103(a)

Claims 1 and 2 stand rejected under 35 U.S.C. §103 as being obvious over Evans *et al.*, 1992, *Journal of Immunological Methods* 156:231-238 ("Evans") of record, in view of U.S. Patent No. 5,840,834 (the "'834 patent"). Claim 3 stands rejected under 35 U.S.C. §103 as being obvious over Evans, in view of the '834 patent as applied to Claims 1 and 2, and further in view of Sevier *et al.*, 1981, *Clinical Chemistry* 27:1797-1806 ("Sevier"). The rejections are respectfully traversed.

In order to make a *prima facie* showing of obviousness, the Examiner bears the initial burden of citing a combination of references that, *inter alia*, teaches or suggests every element of the claimed invention. *See In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). The Examiner must show that the cited references teach or suggest the claimed invention, and that, at the time of the invention, the skilled artisan would have had a reasonable expectation of success that the claimed invention would work. Further, the Examiner cannot, in hindsight, combine references unless the references provide a motivation to do so, and he has to consider the teachings provided by the references as a whole. Applicants submit that the Examiner has failed to meet his burden of establishing a *prima facie* case of obviousness.

The present invention is directed to an antibody against the histidine portion of a fusion polypeptide, wherein the histidine portion of the fusion polypeptide comprises six through eighteen successive histidine residues.

Evans teaches polyclonal antibodies directed to fusion proteins containing metal binding peptides. Specifically, the antibodies are made against a metal binding peptide that comprises three *non-consecutive* histidine residues. Evans, however, does not teach antibodies which bind a metal binding protein containing six to eighteen consecutive histidine residues, as recited in the presently claimed invention.

The Examiner asserts that the shortcoming of Evans is filled in by the '834 patent. Specifically, the Examiner states that "the purpose of the '834 patent was to disclose that other metal binding peptides containing a string of 6-18 histidines were available to make antibodies to, and were previously used in IMAC." *See*, Office Action at page 3. Applicants respectfully submit that the teaching of the '834 patent does not provide the missing elements of Evans.

As previously stated by the Examiner, Evans fails to teach antibodies which bind a histidine portion of a fusion protein, where the histidine portion comprises six to eighteen *consecutive* histidine residues. Applicants respectfully point out that the missing element is not provided by the '834 patent. Indeed, the '834 patent is not concerned with any type of antibodies, let alone antibodies binding the histidine portion of a fusion protein. Accordingly, the '834 patent cannot provide for the missing piece of Evans, -- an antibody that binds a histidine portion comprising six to eighteen consecutive histidine residues. Thus, the combination of Evans and the '834 patent does not teach all the elements of the claimed invention, as required by the law for the advancement of a *prima facie* case of obviousness. Therefore, the rejection of Claims 1 and 2 under 35 U.S.C. §103(a) as being over Evans in view of the '834 patent is in error and should be withdrawn. The rejection of Claim 3 under 35 U.S.C. §103(a) as being over Evans in view of the '834 patent and Sevier should be withdrawn for the same reasons.

Furthermore, as discussed previously, the cited references fail to provide motivation to combine the teachings taught therein. Specifically, Evans is concerned with immunological detection of a metal binding peptide that includes three non-consecutive histidine residues (*His-Asp-His-Asp-His*). The '834 patent, in contrast, uses a histidine tag for the detection of fusion proteins using non-immunological detection methods, namely the organic chelator CM-Lys linked to a peroxidase enzyme. Nothing in the cited references provides motivation to make antibodies against the histidine tag provided by the '834 patent. The teaching of Evans that one can make antibodies against a *His-Asp-His-Asp-His* peptide is completely unrelated to the making of antibodies against a histidine portion comprising between about six and about eighteen *consecutive* histidine residues. Accordingly, the cited references do not provide a motivation to combine the teachings set forth therein. Thus, the combination of references advanced by the Examiner is improper, and the rejection of Claims 1, 2, and 3 under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

In view of the above remarks, the subject application is believed to be in good and proper order for allowance. Early notification to this effect is earnestly solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 493-4935. The commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 16-1150 (order no.8484-029-999) for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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43,341

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APPENDIX A
Pending Claims

1. (Reiterated) An antibody against a fusion polypeptide, wherein said fusion polypeptide comprises a histidine portion, wherein said antibody is directed against said histidine portion, and wherein said histidine portion comprises 6-18 successive histidine residues.

2. (Reiterated) The antibody of Claim 1, wherein said antibody is a polyclonal antibody.

3. (Reiterated) The antibody of Claim 1, wherein said antibody is a monoclonal antibody.

4. (Reiterated) An antibody, wherein said antibody is deposited under ACC 2207 with the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM).